The role of echocardiography in risk stratification of excess weight, hypertensive children

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Abstract

Given the increasing burden of excess weight in pediatric patients and its relationship with blood pressure (BP) levels, we employed echocardiography to identify cardiac changes in a cohort of excess-weight children and the potential additional effect of raised BP. Forty-six excess-weight children and 28 normal weight controls underwent clinical examination, ambulatory blood pressure monitoring (ABPM), and echocardiography. Left ventricular (LV) mass was similar in the two groups when normalizing to body surface area (BSA). LV mass was greater in excess-weight children by normalizing to height to a power of 2.7 (t(58)=3.27, p=0.002, C.I.[1.97, 8.19]) and also to height to a power of 2.16 with a correction factor of 0.09 (t(70.33)=3.98, p<0.001, 95% C.I. [2.5, 7.51]). Left ventricular hypertrophy (LVH), defined as $>45g/m^{2.16}$ was present in 13 participants (28.3%) from the excess weight arm and one participant (3.7%) from the control arm (p=0.012). One excess weight participant (2.17%) exhibited LVH based on the $>51g/m^{2.7}$ threshold and none when LV mass was normalized to BSA. Relative wall thickness (RWT) was significantly higher in the excess weight group (M=0.41, SD=0.5) compared to controls (M=0.38, SD=0.4), t(71)=2.36, p=0.021, C.I. [0.004, 0.049]. Neither LV wall thickness, LV mass, presence of LVH, nor RWT correlated with abnormal BP levels. We could not demonstrate a clear connection between the observed minor changes and BP status. Depending on the severity and duration of exposure to risk factors, an echocardiogram may point out subtle changes in cardiac size and geometry; such features will identify children at greater risk.

Keywords: pediatric, children, excess weight, hypertension, echocardiography, cardiac dimensions, cardiac geometry, LV mass, left ventricular hypertrophy, risk stratification.

Introduction

There is a known connection between excess weight and blood pressure (BP) levels, this relationship being extensively documented in adults [1–3]. The phenomenon has been studied perhaps less intensely in children but is nevertheless well documented in pediatric cohorts [4]. There is also a well-studied effect of the increased afterload brought about by

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arterial hypertension (HTN) on cardiac dimensions, shape, and function [5]. On the other hand, obesity alone may also be responsible for cardiovascular changes, potentially causing an increase in cardiac dimensions and wall thickness, increased left ventricular mass, and cardiac remodeling [6–11].

Given the increasing burden of excess weight in pediatric patients, we employed echocardiography to identify the presence and extent of cardiac changes (in size and geometry) in a cohort of excess weight children compared to normal-weight controls and the potential additional effect of raised blood pressure in this situation.

Material and Methods

We examined 46 excess weight (either overweight or obese) children and 28 normal-weight controls. Subjects in both arms were otherwise healthy. Weight status was assessed according to the Centers for Disease Control and Prevention (CDC) criteria [12] using an online calculator [13]. Excess weight children were then scheduled for clinical visits at 6-month intervals and were followed up for one year.

Auscultatory BP was determined in both arms using an appropriately sized cuff, the higher reading of the two being used for staging. The staging was performed using both the European (EU) and United States (US) published guidelines [14, 15].

Ambulatory blood pressure monitoring (ABPM) was performed using an oscillometric device and an appropriately sized cuff. Participants and parents were advised to maintain normal levels of physical activity while wearing the device. ABPM results were interpreted using the 2014 US recommendations [16].

Standard transthoracic echocardiography (2D, M-mode, color, and spectral Doppler) and Tissue Doppler Imaging were performed. We determined cardiac and great vessel dimensions, systolic and diastolic function parameters and performed an assessment of heart valves.

Left ventricular (LV) outflow tract, end-diastolic septum and LV free wall thickness, end-diastolic and end-systolic LV internal linear dimensions were measured in 2D. LV mass and LV mass index were provided by the echo machine software based on M-mode tracing linear measurements. Subsequently, during database analysis, the LV mass, LV mass index, and relative wall thickness (RWT) were recalculated using 2D-guided linear measurements and an online calculator (available at http://csecho.ca/md-math/?tag=lvmlvmi, accessed May 26th, 2020 [17]).

2D-guided M-mode was employed to calculate fractional shortening (FS) and the ejection fraction using Teichholz's formula. Left atrial volume was calculated using the area-length method. LV end-diastolic and end-systolic volumes were determined using the biplane disc's summation technique. LV ejection fraction was also calculated using the modified Simpson method. We calculated stroke volume and cardiac output.

LV mass was normalized to body surface area, height2.7 [18] and height2.16 + 0.09 [19]. In order to identify the presence of left ventricular hypertrophy (LVH), we employed a threshold of either $115g/m^2$ for boys and $95g/m^2$ for girls, $51g/m^{2.7}$ or $45g/m^{2.16}$ [15, 19]. LV volume was indexed to body surface area. Stroke volume and cardiac output were normalized to body surface area and height to its age-specific allometric power [20]. All other parameters were normalized to body surface area using the Z-score calculator provided by Boston Children's Hospital [21].

Results

Baseline participant characteristics have been reported elsewhere [22].

Blood pressure data

Auscultatory BP readings were recorded for all participants. APBM data was not available for all children: 80.6% (at baseline), 53.8% (at 6 months), and 65% (at 12 months) of results were considered valid and interpreted (mean percentage of valid recordings 83.7%) (further details on measurement method and results have already been reported [22]). In both arms, we found a surprisingly high prevalence of hypertension (HTN) (any stage) at baseline derived from manual measurements: only 53.1% in the excess weight group vs. 21.7% in the control group (p<0.05) according to the European (EU) guidelines [14] and 56.3% vs. 33.3% (p<0.05) according to the United States (US) guidelines [15]. Prevalence was much lower based on ABPM data: 14.3% in the excess weight group vs. only 4% in the control group.

Echocardiographic findings

The mean values recorded for relevant 2D parameters may be found in Tables 1 and 2.

The left ventricle

Regarding left ventricular thickness, normal values were recorded for most participants after standardi-

Table 1. Mean values and standard deviations of various 2D parameters, by age group, in the excess weight arm.

	2–5 years	6–9 years	10–13 years	14–18 years	Total
IVS (mm)	6.32 (±0.74)	7.61 (±0.87)	8.55 (±0.83)	9.97 (±1.15)	8.12 (±1.32)
LVPW (mm)	6.62 (±0.53)	7.51 (±0.84)	8.52 (±0.91)	10.17 (±0.76)	8.23 (±1.3)
LVEDD (mm)	35.1 (±4.05)	36.49 (±2.91)	40.91 (±4.36)	45.55 (±2.64)	39.15 (±4.9)
LVESD (mm)	21.56 (±2.53)	22.35 (±3.08)	25.73 (±2.69)	27.68 (±1.73)	24.25 (±3.46)
LV EDV (ml)	47.48 (±12.78)	45.01 (±11.14)	67.66 (±15.26)	78.7 (±15.92)	58.05 (±18.82)
LV ESV (ml)	20.98 (±3.86)	19.89 (±9.4)	28.54 (±10.59)	27.96 (±6.7)	24.25 (±10)
LA volume (ml)	14.08 (±3.84)	20.76 (±7.56)	27.11 (±6.77)	34.7 (±6.34)	24.29 (±8.97)

IVS – interventricular septum; LVPW, LV posterior wall; LVEDD, LV – end-diastolic diameter; LVESD, LV – end-systolic diameter; EDV – end-diastolic volume; ESV – end-systolic volume; LA – left atrium.

zation: 95.65% of participants from the excess weight group exhibited normal values of both septum and free ventricular wall, while the same can be said for the control group (96.29% and 81.48%, respectively). There was no significant variation according to the hypertensive status.

Left ventricular mass has been indexed (LVMi) in several ways (see above). There was no significant difference between groups by normalizing to body surface area, irrespective of measurements being made with M-mode or 2D. However, LV mass was statistically significantly greater in excess weight children ($M=33.18g/m^{2.7}$, SD=6.7) compared to normal-weight children ($M=28.1 g/m^{2.7}$, DS=4.3) by normalizing to height to a power of 2.7 (t(58)=3.27, p=0.002, C.I.[1.97, 8.19]) and also by indexing to height to a power of 2.16 with a correction factor of 0.09 (t(70.33)=3.98, p<0.001, 95% C.I. [2.5, 7.51]) (Table 3). Within the excess weight group, there was no significant difference of LVMi values according to the presence of HTN, either diagnosed by the manual US, EU standard, or ABPM (Table 4).

Left ventricular hypertrophy (LVH) prevalence according to the $>51g/m^{2.7}$ threshold was very low: a single excess weight participant (2.17%) exhibited LVH.

LVH defined as $>45g/m^{2.16}$ was present in 13 participants (28.3%) included in the study group and one participant (3.7%) in the control group (p=0.012). Its presence did not correlate with abnormal BP (meaning high-normal/elevated BP or frank HTN) or hypertension in the excess weight arm, regardless of diagnostic method (although it came closest to statistical significance when correlated with HTN diagnosed by means of ABPM, p=0.07). The one participant with LVH and normal body weight was deemed hypertensive according to manual measurements, but not according to ABPM. LVH was not present in any of the children when LV mass was normalized to body surface area.

With respect to LV geometry, 26 participants (35.61%) from both groups exhibited increased relative wall thickness (>0.42)[23]. Of these, 20 were overweight (43.47% of the experimental group),

Table 1. Mean values and standard deviations of various 2D parameters, by age group, in the excess weight arm.

	2–5 years	6–9 years	10–13 years	14–18 years	Total
IVS (mm)	5.50 (±0)	6.29 (±0.39)	7.97 (±1.06)	8.16 (±0.80)	7.73 (±1.13)
LVPW (mm)	6.90 (±0)	6.78 (±0.38)	7.95 (±1.24)	8.27 (±0.79)	7.90 (±1.05)
LVEDD (mm)	32.90 (±0)	36.33 (±4.02)	41.44 (±3.15)	42.16 (±2.96)	40.74 (±4.03)
LVESD (mm)	16.60 (±0)	21.40 (±1.27)	25.83 (±2.80)	25.75 (±2.53)	24.79 (±3.3)
LV EDV (ml)	40.80 (±0)	33.58 (±8.03)	70.99 (±24.75)	77.72 (±23.79)	67.25 (±27.17)
LV ESV (ml)	15.20 (±0)	13.62 (±1.24)	27.21 (±12.71)	29.42 (±12.43)	25.76 (±12.71)
LA volume (ml)	15.40 (±0)	20.15 (±5.97)	29.04 (±9.32)	27.81 (±5.81)	26.58 (±7.86)

IVS – interventricular septum; LVPW, LV – posterior wall; LVEDD, LV – end-diastolic diameter; LVESD, LV – end-systolic diameter; EDV – end-diastolic volume; ESV – end-systolic volume; LA – left atrium.

Table 3. Comparison of mean LV mass in the two groups after normalization by various methods.

	Excess weight M (SD)	Controls M (SD)	Statistical significance
LV mass (M-mode) to body surface area (g/m^2)	76.81 (18.92)	72.78 (14.78)	t(44)=0.78 P=0.436 95% C.I. [-6.3,14.37]
LV mass (2D) to body surface area (g/m^2)	61.54 (12.08)	66.04 (12.16)	t(71)= -1.53 P=0.130 95% C.I. [-10.35,1.36]
LV mass (2D) to height$^{2.7}$ (g/m$^{2.7}$) *	33.18 (6.7)	28.1 (4.7)	t(58)=3.27 P=0.002 95% C.I. [1.97,8.19]
LV mass (2D) to height$^{2.16}$ +0.09 (g/m$^{2.6}$)	39.47 (8.06)	34.66 (5.63)	t(68.71)=2.98 P=0.004 95% C.I. [1.59,8.01]

* Indexed only for participants aged >8 years old, in keeping with current recommendations.

and 6 had normal body weight (22.22% of the control group).

Overall, relative wall thickness was significantly higher in the excess weight group (M=0.41, SD=0.5) compared to controls (M=0.38, SD=0.4), t(71)=2.36, p=0.021, C.I. [0.004, 0.049]. However, the difference in the prevalence of concentric remodeling did not reach statistical significance (p=0.058). We also explored a potential connection between the presence of HTN and an increase in RWT. Nevertheless, although RWT was indeed higher in hypertensive children (diagnosed as such by means of ABPM, M=0.41, SD=0.06) compared to children with normal BP (M=0.39, DS=0.04) (the discrepancy being slightly more obvious when examining excess weight children only, M=0.44, SD=0.03 as opposed to M=0.40, SD=0.05), this did not reach statistical significance.

Seven participants included in the excess weight group exhibited concentric hypertrophy (LVH being established after normalization to height2.16).

This, however, did not correlate with the presence of abnormal BP or HTN, regardless of the diagnostic technique.

Discussion

In this cohort, we observed a surprisingly high prevalence of increased BP levels for the age when using manual measurements alone. More insight into this topic may be found elsewhere [22]. However, ABPM appears to be the diagnostic method of choice when available since manual measurements alone can overestimate the prevalence of HTN in children.

Contrary to some previous studies, we did not find any significant dissimilarities of left ventricular thickness across the two groups [24–27]. Moreover, measurements were mostly normal regardless of weight or blood pressure status. One possible

Table 4. Comparison of mean LV mass index (LVMi) in excess weight children with and without arterial hypertension (HTN).

	Normal BP	HTN	P value
Manual, EU			
LVMi g/m$^{2.7}$, M (SD)	32.13 (6.76)	34.24 (7.28)	0.639
LVMi g/m$^{2.16}$, M (SD)	38.03 (8.1)	40.35 (7.94)	0.387
Manual, US			
LVMi g/m$^{2.7}$, M (SD)	33.13 (6.76)	33.98 (7.21)	0.707
LVMi g/m$^{2.16}$, M (SD)	38.03 (8.1)	40.38 (7.98)	0.368
ABPM			
LVMi g/m$^{2.7}$, M (SD)	31.61 (5.6)	34.42 (4.3)	0.35
LVMi g/m$^{2.16}$, M (SD)	37.13 (6.7)	43.08 (6.42)	0.161

M – mean; SD – standard deviation.

explanation could be the young age of the participants (in the excess weight arm, the average age was 10, while the youngest participant was only 3 years old), meaning that, timewise, exposure to the risk factors we examined (excess weight and high blood pressure) was fairly limited. Our data indicate that relative wall thickness may be more useful than 2D linear measurements alone.

Because left ventricular mass will clearly vary with a child's age and development, various indexing methods have been employed over the years to allow proper comparison across age groups; among the most widely used are normalizing LV mass to body surface area, lean body mass, or height to various powers. Along with allowing comparison, indexing also enables utilizing fixed thresholds for diagnosing left ventricular hypertrophy, such as over $51g/m^{2.7}$ (which will place the measurement above the 99th percentile for distributions of LV mass in children and adolescents) or over $38.5g/m^{2.7}$ (above the 95th percentile) [15, 18].

There are pros and cons to all these methods. For instance, some studies (in adults and children) suggest that normalizing to body surface area or lean body mass will underestimate the prevalence of LVH [28, 29]. One study compared indexing to height to a power of 2.7 with other methods and found major discrepancies in LVH prevalence when different normalization techniques were used [18].

Because of these reasons, in this study, we employed multiple normalizing methods. In agreement with previous studies, LV mass indexed to body surface area was similar between groups [18, 28]. When it was normalized to height$^{2.7}$ or height$^{2.16}$ + 0.09 (as described in [18, 19]), LV mass was significantly higher in excess weight children.

Surprisingly, we could not demonstrate a higher LVMi in children with higher BP values. The explanation for this could be the relatively low prevalence (only 14.3%) of HTN confirmed by ABPM. Other reasons could be that blood pressure values were not extremely high (most participants did not require treatment) and, as mentioned before, the relatively short time interval in which HTN was present. To note as a possible incipient change, although it did not reach statistical significance, relative wall thickness was higher in excess weight, hypertensive children.

A higher LV mass did not result in a higher prevalence of left ventricular hypertrophy when indexed to body surface area or height$^{2.7}$ and was only significantly more frequent when normalizing to height$^{2.16}$. This reinforces the discrepancies noted in previous studies and mentioned above; close to one-third of excess weight participants had LVH according to this threshold. Compared to the others, this is a relatively newly described method of normalization.

Although it has been suggested that indexing to height$^{2.16}$ will eliminate false-positive LVH in children [19], in our cohort, it seems to be more sensi-

tive. This could be due to the fact that the $51g/m^{2.7}$ threshold corresponds to the 99th percentile, while the $45g/m^{2.16}$ partition corresponds to the 95th percentile for distributions of LV mass. It is difficult to assess which method would be more appropriate based on our data, and more accurate tests for LVH (such as cardiac magnetic resonance) should be performed in order to draw a conclusion.

The fact that we only observed minor echocardiographic changes and were unable to prove an additional effect of high BP could represent a unique trait of our cohort (small groups, young age, mild phenotype). This makes identifying the individuals who exhibit these features all the more important since they are more likely to be high-risk (it has been shown that increased cardiac dimensions during childhood may track into young adulthood [30]). The advantage is that echocardiography is widely available, inexpensive, and safe. Moreover, LV mass and geometry parameters are easily calculated from standard measurements.

Performing a standard echocardiogram early on could thus offer a window of opportunity to accurately identify these children and take appropriate measures in order to prevent more definite structural cardiac changes from occurring.

Conclusion

Although minor structural changes were recorded in the excess weight group, we could not demonstrate a clear connection with blood pressure status. However, depending on severity and duration of exposure to risk factors, an echocardiogram may point out subtle changes such as an increased left ventricular mass index, increased relative wall thickness or, as things progress, cardiac remodeling (mostly of the concentric type) and even left ventricular hypertrophy.

Identifying such changes during standard echocardiography will single out children at greater risk, needing closer follow-up and more stringent lifestyle measures.

Acknowledgement

Conflict of interest

The authors confirm that there are no conflicts of interest.

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